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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/913,967 | 12/31/2001 | Wilhelmus Evergardu Hennink | 313632001000 | 8024 |

25225 7590 02/12/2007

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

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| EXAMINER |
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FUBARA, BLESSING M

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| ART UNIT | PAPER NUMBER |
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1618

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS | 02/12/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/913,967

Applicant(s)

HENNINK ET AL.

Examiner

Blessing M. Fubara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2006.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 21-26 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-17 and 21-26 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 11/17/06.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, IDS, amendment and remarks, all filed 11/17/06. Claim is amended. Claims 1-17 and 21-26 are pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-10, 14 and 21-26 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hennink et al. (WO 98/00170, cited on form PTO-1449).

Hennink discloses a biodegradable hydrogel that contains hydrolysable bonds and where the hydrogel consists of two interpenetrating polymer networks interconnecting to one another through hydrolysable spacers (abstract). In Hennink, (poly)glycolic acid and/or (poly)lactic acid spacers are introduced between polymerizable methacrylate groups and dextran (page 7, lines 24-27 and page 8). The hydrogel is prepared by a radical polymerization in the presence of tertiary amine and persulfate initiator (page 9, lines 14-23). Increasing degree of substitution (DS) yields a more cross-linked network (page 9, lines 31-34). Drugs are loaded onto the

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hydrogel during polymerization or cross-linking (page 10, lines 24 and 25). The hydrogel of Hennink are applied as microspheres of varying sizes (page 10, lines 26-34). See also examples 1-5 for preparation of hydrogels. The teachings of Hennink meet the limitations of the claims.

“When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Response to Arguments

3. Applicants' arguments filed 11/17/06 have been fully considered but they are not persuasive.

Applicant argues that Hennink does not disclose two polymers that are substituted with chiral oligomers; applicant's first and second points in the argument are the same with each stating that the prior art of Hennink does not disclose two polymer strands.

Response:

Regarding the absence of specific chirality in Hennink, it is noted that the prior art meets the limitation of the oligomers recited in claim 2, which defines the oligomers of claim 1. A racemic molecule has equal components of each component of the opposite chirality. Regarding specific claimed chirality, it is noted that the composition claims do not exclude or include covalent or non-covalent interaction. Furthermore, the composition is a blend of A and B, where the hydrophilic polymer in A is not different from that in B, so that within the blend is present a racemic the hydrophilic polymer and the oligomers of lactic or glycolic acids. Further still, Hennink discloses that the composition comprises two interpenetrating polymer networks (claims 2). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” In re

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Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, Hennink anticipates claim 1 and claims 2-10, 14 and 21-26.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 11-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hennink et al. (WO 98/00170, cited on form PTO-1449).

Hennink clearly teaches the instant hydrogel composition. Hennink teaches that increasing degree of substitution (DS) yields a more cross-linked network (page 9, lines 31-34). As it regards claim 12, Hennink discloses that the hydrophilic polymer contains polylactic or polyglycolic acid and Hennink specifically describes the presence of one or more units of the

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lactic or glycolic acid (page 9, line 12) so that lactic acid or glycolic acid used in Hennink would have one or more units of the acid that would provide the desired release of the incorporated active upon hydrolysis/degradation of the lactic or glycolic. Regarding claim 13, Hennink is silent on the length of the oligomeric groups and it flows that a racemic mixture of lactic acid or glycolic acid would have equal lengths such that in the combination is racemic. Hennink does not teach a degree of substitution of 3-25 as recited in instant claim 11. There is no comparable example to demonstrate that a degree of substitution of 3-25 provides unusual results.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a stereocomplex hydrogel that has appropriate degree of substitution since according to the teaching of Hennink degree of substitution is related to how cross-linked the polymer network is. One having ordinary skill in the art would have been motivated to prepare a stereocomplex hydrogel composition with a varying degree of substitution with the expectation of obtaining a hydrogel with the desired cross-linked network.

7. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Jong et al. (Macromolecules, 1998, 31:6397-6402, provided by applicants on form PTO-1449) in view of Brannon-Peppas (Int. J. Pharm., 1995, 116:1-9, provided by applicants on form PTO-1449).

De Jong discloses preparation of stereocomplexes homo- or copolymers of D- and L-lactides and further discloses that stereocomplex formation is also observed in blends of L-lactide/s-caprolactone and D-lactide/E-caprolactone (abstract and page 6397). Synthesis of the stereocomplex begins with preparing the oligomer in the presence (2-methoxyethoxyethanol (MEE)) initiator and stannous octoate catalyst (page 6399).

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De Jong does not teach incorporating active ingredient in the stereocomplex. However, Brannon-Peppas discloses that copolymers of polylactic acid are drug carriers (abstract). Regarding the sequence or preparing the drug containing hydrogel, selection of any order of the preparation steps in instant claims 15-17 is obvious in the absence of unexpected results showing that the order recited in the claims provides unusual results. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include an active ingredient in the hydrogel composition of De Jong since Brannon-Peppas teaches that lactide hydrogels can be drug carriers. One having ordinary skill in the art would have been motivated to include active agents in the lactide hydrogel formulation of De Jong with the expectation that the stereocomplex lactide hydrogel would serve as a carrier.

Response to Arguments

8. Applicants' arguments filed 11/17/06 have been fully considered but they are not persuasive.

Applicant argues that

a) Hennink cannot render claims 11-13 obvious because, Hennink does not suggest polymers that are substituted with complementary chiral groups that interact noncovalently.

Response:

The response given above for Hennink shows that a racemic mixture contains equal amounts of the L and D-forms of the acids and therefore, Hennink anticipates the claims and renders obvious the claims as described above. Claims 11 and 12 are directed to mixtures of lactic acid polymers.

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b) that De Jong employs poly disperse lactic acid oligomers prepared by using 2-(2-methoxyethoxy)ethanol as initiator and stannous octoate as catalyst; that the stereocomplexes of De Jong are not hydrogels according to Professor Hennink's declaration; that there is no motivation to combine Brannon-Peppas with De Jong because Brannon-Peppas does not overcome the deficiency of De Jong and neither of the two references disclose two water soluble or water dispersible hydrophilic polymers.

Response:

The initiator 2-(2-methoxyethoxy)ethanol and catalyst stannous octoate meet the generic recitation of suitable initiator. Claim 13 does not exclude using 2-(2-methoxyethoxy)ethanol as initiator and stannous octoate as catalyst since no specific initiator and catalyst are recited in the claims. Claim 13 is the process of preparing a hydrogel by polymerizing a monomer and in this case De Jong discloses lactide monomers (see applicant's specification at page 41, lines 22-25). Since De Jong uses the same components in its process as for the claimed process, it flows that the product formed from the same starting materials using same initiators would yield hydrogel. Therefore, Brannon-Peppas does not have to overcome hydrogel deficiency because the product formed by the process of De Jong is inherently a hydrogel. The motivation to combine Brannon-Peppas with De-Jong is found in Brannon-Peppas disclosure that copolymers of polylactic acid are used as drug carriers and Brannon-Peppas makes up for the deficiency that De-Jong does not have drug incorporated in the hydrogel product.

The declaration by Professor Hennink was previously addressed and noted that the declaration is not commensurate with the invention in terms of formation of hydrogel **only** in water because applicant's Example 1, for example, is prepared in organic solvent and applicant's examples 1, 2 and 4 appear to contradict Exhibit 3 submitted with the declaration.

No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech, Center 1600

BF


MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER